CLAIMS

WHAT IS CLAIMED IS:

1. A method for parallel synthesis of an array of selected multimers on a substrate comprising isolated reaction sites containing one or more protected initiating moieties, the method comprising:

   (a) selectively irradiating isolated reaction sites to generate deprotected initiating moieties at the irradiated isolated reaction sites;

   (b) coupling one or more monomers to the deprotected initiating moieties;

   (c) repeating steps (a) — (b) until the array of selected multimers has been synthesized;

   wherein the multimers synthesized comprise multimers from about 75 to 200 monomers is length.

2. The method of claim 1, wherein the multimers synthesized comprise multimers from about 100 to 125 monomers is length.

3. The method of claim 1, wherein the selected multimers are DNA.

4. The method of claim 1, wherein the selected multimers are oligonucleotides.

5. The method of claim 1, wherein the selected multimers are RNA.

6. The method of claim 1, wherein the selected multimers are DNA/RNA hybrids.

7. The method of claim 1, wherein the selected multimers are peptides.

8. The method of claim 1, wherein the selected multimers are carbohydrates.

9. The method of claim 1, wherein the deprotected initiating moieties are generated by:

   (a) contacting the substrate with a liquid solution comprising one or more photo-reagent precursors, such that the liquid solution is in contact with the initiating moieties;

(b) selectively irradiating isolated reaction sites to produce one or more photo-generated reagents, wherein the photo-generated reagents are effective to deprotect the initiating moieties at the irradiated isolated reaction sites.

10. The method of claim 10, wherein the photo-reagent precursors are selected from the group consisting of acid precursors and base precursors.

11. The method of claim 1, wherein the monomer comprises an unprotected reactive site and a protected reactive site.

12. The method of claim 1, where in the monomer is selected from the group consisting of nucleophosphoramidites, nucleophosphonates and analogs thereof.

13. The method of claim 1, wherein the protected initiating moieties are protected by an acid-labile group.

14. The method of claim 1, wherein the protected initiating moieties comprise linker molecules, wherein each of the linker molecules comprise a reactive functional group protected by an acid-labile group.

15. A method of generating a DNA sequence comprising:

selecting suitable oligonucleotide subchains for the assembly of the DNA sequence, wherein the subchains are designed so that the DNA sequence is formed by the annealed subchains;

parallel synthesis of the subchains on a solid support, wherein the subchains are from about 75 to about 150 nucleotides in length;

annealing the subchains;

ligating the annealed subchains to generate the DNA sequence.

16. The method of claim 15, wherein the DNA sequence is 100 bp to 1,000 bp in length.

17. The method of claim 15, wherein the DNA sequence is 1,000 bp to 10,000 bp in length.

18. The method of claim 15, wherein the DNA sequence is selected from the group consisting of genes, gene fragments, transposons, regulatory regions, transcription machines, expression constructs, gene therapy constructs, homologous recombination constructs, vaccine constructs, viral genomes, vectors, and artificial chromosomes.

19. The method of claim 15, wherein the subchains are cleaved from the solid support before the subchains are annealed.

20. The method of claim 19, wherein predetermined subchains are cleaved from the solid support before the subchains are annealed.

21. The method of claim 20, wherein the predetermined subchains are annealed to subchains attached to the solid support.

22. The method of claim 20, wherein the subchains are cleaved from the solid support using a restriction endonuclease enzyme.

23. The method of claim 15, wherein the oligonucleotide subchains comprise one or more reverse-U linkers.

24. The method of claim 23, wherein the oligonucleotide subchains are cleaved from the solid support using RNase A.

25. The method of claim 15, wherein the oligonucleotide subchains are designed so that gaps are present in the duplex DNA sequence formed by the annealed subchains.

26. The method of claim 25, wherein the gaps present in the duplex DNA sequence are filled in with a DNA polymerase.

27. A method of generating a DNA sequence comprising:

a) selecting suitable oligonucleotide subchains for the assembly of the DNA sequence, wherein the subchains are designed so that the duplex DNA sequence is formed by the annealed subchains;

b) parallel synthesis of the subchains on a solid support, wherein a 98% coupling efficiency or greater per step of oligonucleotide synthesis is achieved;

c) annealing the subchains;

d) ligating the annealed subchains to generate the DNA sequence.

28. A method of generating a library of short RNA molecules comprising:

a) synthesizing an array of selected oligonucleotides on a substrate, wherein the selected oligonucleotides comprise an RNA polymerase promoter sequence, wherein the substrate comprises protected initiating moieties at specific reaction sites on the substrate, comprising:

i) contacting the substrate with a liquid solution comprising one or more photo-reagent precursors, such that the liquid solution is in contact with the protected initiating moieties;

ii) isolating the specific reaction sites;

iii) selectively irradiating isolated reaction sites to produce one or more photo-generated reagents, wherein the photo-generated reagents are effective to deprotect the initiating moieties at the irradiated reaction sites;

iv) contacting the substrate with a monomer, wherein the monomer comprises an unprotected reactive site and a protected reactive site, under conditions such that the unprotected reactive site of the monomer couples with the deprotected initiating moieties so as to create an attached monomer and protected initiating moieties;

v) repeating steps (i) — (iv) until the array of selected oligonucleotides has been synthesized;

wherein the selected oligonucleotides comprise two specific primer sequences for DNA amplification;

b) cleaving of the selected oligonucleotides from the solid support;

c) amplifying the selected oligonucleotides using primers that recognize the specific primer sequences, wherein double stranded DNA comprising the sequences of the selected oligonucleotides is generated;

d) *in vitro* transcription of the amplified double stranded DNA using an RNA polymerase that recognizes the RNA promoter sequence, wherein a library of short RNA molecules is generated.

29. The method of claim 28, wherein the short RNA molecules are short interfering RNA (siRNA) molecules.

30. The method of claim 28, wherein the selected oligonucleotides comprise one or more reverse-U linkers.

31. The method of claim 31, wherein the selected oligonucleotides are cleaved from the solid support using RNase A.

32. The method of claim 28, wherein the selected oligonucleotide comprise one or more restriction enzyme sites.

33. The method of claim 28, wherein the RNA polymerase is selected from the group consisting of T7 RNA polymerase, SP6 RNA polymerase, and T3 RNA polymerase.

34. A method of large-scale Single Nucleotide Polymorphism (SNP) detection in a DNA sample comprising:

a) designing an array of primer pairs that will amplify an array of amplicons from the DNA sample, wherein each amplicon comprises one or more SNPs;

b) synthesizing the array of primer pairs on a substrate, wherein the substrate comprises protected initiating moieties at specific reaction sites on the substrate, comprising:

i) contacting the substrate with a liquid solution comprising one or more photo-reagent precursors, such that the liquid solution is in contact with the protected initiating moieties;

ii) isolating the specific reaction sites;

iii) selectively irradiating isolated reaction sites to produce one or more photo-generated reagents, wherein the photo-generated reagents are effective to deprotect the initiating moieties at the irradiated reaction sites;

iv) contacting the substrate with a monomer, wherein the monomer comprising an unprotected reactive site and a protected reactive site, under conditions such that the unprotected reactive site of the monomer couples with the deprotected initiating moieties so as to create an attached monomer and protected initiating moieties;

v) repeating steps (i) — (iv) until the array of selected oligonucleotides has been synthesized;

wherein a single primer pair is synthesized in each reaction site on the substrate;

b) DNA amplification of the amplicons using the primer pairs, wherein a single amplicon is generated in each reaction site on the substrate;

c) detection of the one or more SNPs present in each amplicon.

35. The method of claim 34, wherein the one or more SNPs present in each amplicon are detected by PCR, Oligonucleotide Ligation Assay (OLA), mismatch hybridization, Single Base Extension Assay, RFLP detection based on allele-specific restriction-endonuclease cleavage, or hybridization with allele-specific oligonucleotide probes.

36. A method of large-scale Single Nucleotide Polymorphism (SNP) detection in a DNA sample comprising:

a) designing an array of primer pairs that will amplify an array of amplicons from the DNA sample, wherein each primer pair will only amplify an amplicon if a particular SNP is present in the DNA sample;

b) synthesizing the array of primer pairs on a substrate, wherein the substrate comprises protected initiating moieties at specific reaction sites on the substrate, comprising:

i) contacting the substrate with a liquid solution comprising one or more photo-reagent precursors, such that the liquid solution is in contact with the protected initiating moieties;

ii) isolating the specific reaction sites;

iii) selectively irradiating isolated reaction sites to produce one or more photo-generated reagents, wherein the photo-generated reagents are effective to deprotect the initiating moieties at the irradiated reaction sites;

iv) contacting the substrate with a monomer, wherein the monomer comprising an unprotected reactive site and a protected reactive site, under conditions such that the unprotected reactive site of the monomer couples with the deprotected initiating moieties so as to create an attached monomer and protected initiating moieties;

v) repeating steps (i) — (iv) until the array of selected oligonucleotides has been synthesized;

wherein a single primer pair is synthesized in each reaction site on the substrate;

b) DNA amplification of the amplicons using the primer pairs, wherein the amplification of an amplicon indicates the presence of a particular SNP in the DNA sample.

37. A method of generating an oligonucleotide library comprising:

a) synthesizing an array of selected oligonucleotides on a substrate, wherein the selected oligonucleotides comprise two specific primer sequences and a variable region of sequence, wherein the substrate comprises protected initiating moieties at specific reaction sites on the substrate, comprising:

i) contacting the substrate with a liquid solution comprising one or more photo-reagent precursors, such that the liquid solution is in contact with the protected initiating moieties;

ii) isolating the specific reaction sites;

iii) selectively irradiating isolated reaction sites to produce one or more photo-generated reagents, wherein the photo-generated reagents are effective to deprotect the initiating moieties at the irradiated reaction sites;

iv) contacting the substrate with a monomer, wherein the monomer comprising an unprotected reactive site and a protected reactive site, under conditions such that the unprotected reactive site of the monomer couples with the deprotected initiating moieties so as to create an attached monomer and protected initiating moieties;

v) repeating steps (i) — (iv) until the array of selected oligonucleotides has been synthesized;

b) cleavage of the selected oligonucleotides from the solid support;

c) DNA amplification of the selected oligonucleotides using primers that recognize the specific primer sequences, thereby generating an oligonucleotide library of double stranded DNA sequences comprising the variable region sequences of the selected oligonucleotides.